Draft Guidance for FDA Staff

Male Condom Defects (CPG 7124.21)

Document Release Date: [date of FR Notice]

U.S. Department of Health and Human Services
Food and Drug Administration
Office of Regulatory Affairs
Office of Enforcement
Division of Compliance Policy

02D-0103

GDL-1

Preface

Public Comment:

Written comments regarding this document may be submitted to the Dockets Management Branch (HFA-305), Food and Drug Administration, 5630 Fishers Lane, rm. 1061, Rockville, MD 20852. Submit electronic comments to http://www.fda.gov/dockets/ecomments. For questions regarding the use or interpretation of this guidance, contact John Farnham at 301-594-4618, ext. 117.

Additional Copies:

Submit written requests for a single copy of the guidance to the Division of Small Manufacturers, International and Consumer Assistance (HFZ-220), Center for Devices and Radiological Health, Food and Drug Administration, 1350 Piccard Drive, Rockville, MD 20850, or FAX your request to 301-443-8818. A copy of the guidance may also be downloaded to a personal computer with access to the Internet. The Office of Regulatory Affairs' (ORA) home page includes the guidance and may be accessed at "http://www.fda.gov/ora". The guidance is available under "Compliance References."

Compliance Policy Guide

Draft Guidance

This draft guidance document represents the agency's current thinking on male condom defects. It does not create or confer any rights for or on any person and does not operate to bind FDA or the public. An alternative approach may be used if such approach satisfies the requirements of the applicable statute, regulations, or both.

Sub Chapter 345
Obstetrics and Gynecology

Sec. 345.100 Male Condom Defects (CPG 7124.21)

BACKGROUND:

1. FDA Water Leak Testing

The Food and Drug Administration (FDA) has had a long history of seizure actions against male condoms because of defects detected by water leak testing. Such leakage defects clearly indicate the failure of individual condoms to provide an adequate barrier. In 1987, FDA modified an earlier version of this guidance entitled "Compliance Policy Guide Condoms; Defects – Criteria for Direct Reference Seizure (CPG 7124.21)" so that the factors considered for determining adulteration of condom lots would parallel the American Society for Testing Materials (ASTM) standard that is currently entitled "Designation: D3492 ... Standard Specification for Rubber Contraceptives (Male Condoms)," (ASTM D3492). This is the voluntary standard that is used by domestic latex condom manufacturers to assess the quality of their products. In 1987, when this guidance was modified to parallel the ASTM standard, the Acceptable Quality Level (AQL) for leakage was 0.4 (i. e. manufacturers' process average defect rate should not exceed 0.4%, or 4 leaking condoms per 1,000 condoms produced).

As part of the process mandated by the FDA Modernization Act of 1997, Section 514 (c) of the Federal Food, Drug, and Cosmetic Act, the FDA now recognizes parts of ASTM D3492, as well as the International Organization for Standardization (ISO) standard for "Rubber Condoms" (ISO 4074), for the purpose of premarket clearance. The scope of the agency's recognition of these standards is described in the supplementary information sheets that are posted on the FDA Internet site at http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfStandards/search.cfm. These information sheets are available when the category "ObGyn/Gastroenterology" is entered in the search criteria. Currently, the supplementary information sheets recognize the

portions of the ASTM and ISO condom standards that contain AQL values for water leak testing. These AQL values have been lowered to 0.25 from the previous value of 0.4 by both ISO and ASTM in order to provide greater assurance of barrier integrity.

To be consistent with current industry practice, the FDA intends to use the AQL identified in the recognized consensus standards as guidance for testing, surveillance, and compliance purposes, as well as for premarket clearance. Therefore, this revised guidance reflects the 0.25 AQL in the currently recognized revisions of these voluntary standards. The current value of the recognized AQL is reflected in the Water Leak Test Sampling Inspection Plan provided in Attachment A. Note that this sampling plan is applicable to FDA water leak testing of male condoms made from either latex or synthetic material, although the actual test methods may differ for synthetic materials (see "Test Methods" below).

FDA has based the Water Leak Test Sampling Inspection Plan on ISO 2859 Part 1, "Sampling Procedures and Tables for Inspection by Attributes," which replaces the former MIL-STD-105E. Single sampling with normal inspection should be used for small lots. For normal size and larger lots, multiple sampling with normal inspection should be used.

2. FDA Air Burst Testing

The water leak test effectively detects holes in condoms, but it cannot provide assurance that condoms will have adequate strength to resist breakage during use. The air burst testing procedures in the ISO 4074 and the ASTM D3492 standards place stress on latex condoms until they fail, and provide a measure of the elasticity and strength of the latex condoms tested. Many studies report that the breakage rate of condoms during use is considerably higher than the established typical condom leakage rates. Therefore, the ability of condoms to resist breakage is a matter of major concern.

As a result, air burst testing requirements for latex condoms were adopted by many countries, including Canada, Australia, and member countries of the European Union. For condoms destined for the United States (U.S.) market, the FDA is likewise concerned with the ability of latex condoms to resist breakage.

On April 5, 1994, FDA's Center for Devices and Radiological Health (CDRH) issued a letter to latex condom manufacturers requesting that they adopt ISO air burst testing as part of their finished device testing to provide increased assurance of protection from sexually transmitted diseases, including Human Immunodeficiency Virus (HIV). Following the issuance of this letter, and the recognition of the ISO 4074, ASTM D3492, and similar standards, all manufacturers of male latex condoms intended for distribution in the U.S. should have established and implemented air burst test requirements as part of their good manufacturing practice (GMP) procedures (21 CFR Part 820).

In the letter issued on April 5, 1994, the FDA also expressed its intention to add air burst testing to its test program for latex condoms. FDA now recognizes the ISO 4074 air burst

standard and portions of the ASTM D3492 air burst standard for the purpose of premarket clearance, and has obtained equipment, and developed test protocols and acceptance guidelines to parallel these standards. This guidance now includes air burst testing of condoms as another factor that the FDA may use to determine whether latex condoms are adulterated.

The Air Burst Test Sampling Inspection Plan contained in Attachment B is based on the Tables for Inspection by Attributes found in ISO 2859-1 for an AQL of 1.0. This is accomplished by assigning to each tested condom the "attribute" that it either does or does not meet the air burst test in the recognized standards.

REGULATORY ACTION GUIDANCE:

When determining whether to pursue enforcement actions for condom lots, the agency must consider all information relevant to possible charges of adulteration and misbranding. This information is not limited to the defect rate of the test sample and the acceptance number under the sampling plans in Attachments A and B, but includes all compelling reasons for either pursuing or not pursuing the action.

A) Condom Lots above the 0.25 AQL for the Water Leak Test

Lots of condoms that are rejected as per the Water Leak Test Sampling Inspection Plan (Attachment A) may be considered adulterated and misbranded, as described below, and may be subject to direct reference seizure. Districts should forward seizure recommendations to the Division of Compliance Management and Operations (HFC-210).

Specimen Charges:

Note: Charges for seizure of devices do not include allegations of shipment in interstate commerce because allegations of interstate commerce are not required to support seizure of devices [see section 304(a)(2)], and FDA's jurisdiction to bring enforcement actions involving devices is presumed under section 709 of the Federal Food, Drug, and Cosmetic Act (the Act).

1. For lots that FDA determines are adulterated on the basis of the water leak test AQL or other factors charge:

   "That the article of device is adulterated within the meaning of the Act, 21 U.S.C. 351(c), in that it is not subject to 21 U.S.C. 351(b) and its quality falls below that which it purports or is represented to possess in that the devices contain defects/holes."

2. If the condoms contain holes and are labeled for the prevention of pregnancy, and FDA is charging a violation of 21 U.S.C. 351(c), FDA may also charge:

"That the article of device is misbranded within the meaning of the Act, 21 U.S.C. 352(a), in that its labeling (for the prevention of pregnancy) is false or misleading, because the labeling fails to reveal a material fact in light of such representations, that the article contains holes."

3. If the lot to be seized was repacked by the dealer, and it is believed that holes may have occurred during repacking, add a statement to the examination paragraph of the complaint similar to the following:

   "(Insert name of firm) repacked the article of device from bulk stock after receipt in interstate commerce."

B) Latex Condom Lots above the 1.0 AQL for the Air Burst Test

Lots of latex condoms should meet the lot acceptance numbers stated in the guidance of the Air Burst Test Sampling Inspection Plan (Attachment B) for the parameters of bursting pressure and bursting volume. Latex condom lots that do not meet the lot acceptance numbers stated in this guidance may be adulterated within the meaning of 21 U.S.C. 351(h), (i.e., failure to meet the GMP requirements). Under some circumstances, CDRH may also determine that these condoms are further adulterated within the meaning of 21 U.S.C. 351(c) for failure to have the quality they purport to possess. The analyses for these unacceptable lots should be forwarded to CDRH's Office of Compliance (HFZ-332), who will determine whether they are adulterated and whether regulatory or administrative actions are appropriate. If necessary, CDRH will consult with the Office of Regulatory Affair's (ORA) Division of Field Science (DFS) to interpret the test results, or to assess whether further testing is needed.

If further action is deemed necessary in order to achieve conformance with the GMP requirements, or to assure the quality of the product, CDRH will coordinate and/or initiate such actions. Actions may include, but are not limited to, the issuance of untitled letters, warning letters, import detentions without physical examination and seizures.

SAMPLE COLLECTION:

For FDA's sampling purposes, a "lot" of condoms should be considered to be "a group of condoms of the same type, class, size and composition, which are associated by manufacture under essentially the same conditions, at essentially the same time." When manufacturing dates or conditions cannot easily be determined, a "sampling lot" should be considered to be "a group of condoms of the same type, class, size and composition, which are associated by conditions of storage or shipment."

These definitions parallel the definition in ISO 2859 except that the ISO definition includes that the products are manufactured under the same conditions at the same time and makes no reference to shipping and storage. These differences reflect different usage of the standard by manufacturers who are testing unshipped product with a known manufacturing history, as compared with usage by FDA which often must sample

products of undetermined manufacturing history but a shared history of shipment or storage.

Field personnel should collect only condoms of one type (brand), class (style), size, and composition (material) in each sample. Common styles of condoms include "unlubricated," "lubricated," "lubricated with spermicide," "super thin," "ribbed," and "extra strength." Different styles and brands of condoms should not be mixed together in a single sample. If more than one style or brand requires testing, then a separate sample should be taken for each style or brand. Clearly, latex condoms and polyurethane condoms would have different compositions and would therefore not be mixed in a sample. However, condoms that differ only in color may also be considered to be of different compositions and should also be sampled separately unless information is available from the premarket notification (510(k)) that indicates that color makes no difference in device performance.

Field personnel should attempt to maintain a single manufacturer lot code throughout a given sample; however, it is important to sample from an adequate number of cartons in order to obtain a representative sample of the chosen style, brand, and composition. Therefore, if it is not feasible to find enough cartons with the same manufacturer lot code, several lot codes of the same style, brand, and composition may be mixed together in one sample. If several lot codes are mixed in a given sample, then the lot size for sampling purposes should be the sum of the manufacturer lot quantities for all lot codes represented in the sample. If the individual manufacturer lot code quantities cannot be determined, the sample size can be based on the total number of condoms of the chosen style, brand, and composition that were received and stored together at the facility.

Field personnel should collect the condoms randomly and representatively from at least 6 shipping cartons, if available, of the condom sampling lot to be tested. The number of condoms to be collected should account for the lot size as well as whether water leak testing, air burst testing, or both types of testing are contemplated. The sample sizes shown in the table below should be appropriate for testing and collection.

Important Note: Unless directed otherwise by ORA headquarters, districts should not collect any "routine" air burst samples for surveillance purposes. However, air burst test samples may be requested on a "for cause" basis by CDRH or by districts in consultation with CDRH.

SIZE OF SAMPLING LOT (NUMBER OF CONDOMS)	SAMPLE SIZES WATER LEAK ONLY *TEST/COLLECT	SAMPLE SIZES AIR BURST ONLY *TEST/COLLECT	SAMPLE SIZES COMBINED AIR/WATER SAMPLE *TEST/COLLECT

51 –1,200	32/36 (3 dozen)	20/36 (3 dozen)	52/72 (6 dozen)
1,201 – 10,000	125/144 (1 gross)	80/96 (8 dozen)	205/240 (20 dozen)
10,001 – 150,000	350/432 (3 gross)	200/288 (2 gross)	550/576 (4 gross)
150,001 – 500,000	560/576 (4 gross)	315/432 (3 gross)	875/1,008 (7 gross)
500,001 – Over	875/1,008 (7 gross)	500/576 (4 gross)	1,375/1,440 (10 gross)

*All sample sizes listed in parentheses above are included as an accommodation to the industry's quantitative packaging practices, and consist of more condoms than may be tested under the sample inspection plans below. For air burst testing, some of the excess condoms may be needed to perform width measurements for calculating the burst volume target value.

TEST METHODS:

FDA water leak testing of male latex condoms should be performed according to the methods detailed in the Laboratory Information Bulletin (LIB) No. 4176. Testing of male condoms made from synthetic materials should be performed according to the methods detailed in LIB No. 4074. Both of these LIB methods include a roll test on a paper towel.

Air burst testing should be conducted as described in part 6 of the ISO 4074 standard (except as noted below in Attachment B regarding condoms that leak instead of bursting). Test protocols may vary depending on the specific test apparatus used.

Attachment A

Water Leak Test Sampling Inspection Plan

Two single and three multiple sample examination plans are presented below for various lot sizes. These plans are based on an AQL of 0.25 per ASTM D3492 and ISO 4074 standards. The inspection level corresponds to level II for lots of 10,000 and under. The inspection level is level I for lots greater than 10,000. Examination may cease when the lot exceeds the reject guidance.

Note: Condoms that appear to have been crimped/damaged in the process of packaging should not be excluded from sampling and analysis.

Single Sample (Water Leak) Plan for Lot Size 51 – 1,200

Number of Condoms Tested	Number of Defective Condoms Accept	Reject

32	0	1

Single Sample (Water Leak) Plan for Lot Size 1,201 – 10,000

Number of Condoms Tested	Number of Defective Condoms Accept	Reject
125	1	2

Multiple Sample (Water Leak) Plan for Lot Size 10,001 – 150,000

Number of Condoms Tested	Cumulative	Number of Defective Condoms Accept	Reject
1st 50	50	X*	2
2nd 50	100	X*	2
3rd 50	150	0	2
4th 50	200	0	3
5th 50	250	1	3
6th 50	300	1	3
7th 50	350	2	3

* Acceptance may not be possible at this stage.

Multiple Sample (Water Leak) Plan for Lot Size 150,001 – 500,000

Number of Condoms Tested	Cumulative	Number of Defective Condoms Accept	Reject
1st 80	80	X*	2
2nd 80	160	0	3
3rd 80	240	0	3
4th 80	320	1	4
5th 80	400	2	4
6th 80	480	3	5
7th 80	560	4	5

* Acceptance may not be possible at this stage.

Multiple Sample (Water Leak) Plan for Lot Size 500,001 and Greater

Number of Condoms Tested	Cumulative	Number of Defective Condoms Accept	Reject
1st 125	125	X*	2

2nd 125	250	0	3
3rd 125	375	1	4
4th 125	500	2	5
5th 125	625	3	6
6th 125	750	4	6
7th 125	875	6	7

* Acceptance may not be possible at this stage.

Attachment B

Air Burst Test Sampling Inspection Plan

Five single sample plans for normal inspection are presented below for various lot sizes. These plans are based on an AQL of 1.0 and on general inspection level I. Examination should proceed until the total number of latex condoms specified by the sampling plan has been tested. (This will provide the most accurate estimate of the failure rate for the sample, which may be considered when determining adulteration).

The actual pressure and volume test values obtained for each condom at the moment of bursting should meet the following target values:

Bursting Pressure - not less than 1.0 kiloPascals

Bursting Volume - not less than $0.00592 \times w^2$ liters (rounded to the nearest 0.5 liter)

where w is the average (laid flat) width of 13 condoms in millimeters (mm) measured at a distance of 70mm ± 5mm from the open end.

Test values of bursting pressure or bursting volume that are below these target values should be counted as failures. The total number of pressure or volume failures (see note 2 below) in the sample should then be used to evaluate the acceptability of the lot as follows:

Single Sample (Air Burst) Plan for Lot Size 51 – 1,200

Number of Condoms Tested	Maximum Number of Pressure or Volume Failures for Lot Acceptance
20	0

Single Sample (Air Burst) Plan for Lot Size 1,201 – 10,000

Number of Condoms Tested	Maximum Number of Pressure or Volume Failures for Lot Acceptance

80	2

Single Sample (Air Burst) Plan for Lot Size 10,001 – 150,000

Number of Condoms Tested	Maximum Number of Pressure or Volume Failures for Lot Acceptance
200	5

Single Sample (Air Burst) Plan for Lot Size 150,001 – 500,000

Number of Condoms Tested	Maximum Number of Pressure or Volume Failures for Lot Acceptance
315	7

Single Sample (Air Burst) Plan for Lot Size 500,001 and Greater

Number of Condoms Tested	Maximum Number of Pressure or Volume Failures for Lot Acceptance
500	10

Note 1: The "Maximum Number of Pressure or Volume Failures for Lot Acceptance" is the maximum number of latex condoms from the sampled lot which can fail the pressure or volume guidance according to the ISO 4074 standard. Sampled lots that exceed this number of failures may be considered adulterated as described above under "Regulatory Action Guidance."

Note 2: When evaluating conformance with the bursting pressure and bursting volume guidance, the volume failures and pressure failures should be evaluated independently, and should not be added together.

Note 3: A condom that leaks during the test, but that does not burst, should not be considered a valid sample test, and should be replaced with another condom.